To comply with the requirements of 35 U.S.C. § 112, second paragraph, a claim need only be understandable to those of skill in the relevant art and need only be reasonably definite. A claim is to be understood in light of the specification. Breadth in a claim does not make a claim indefinite. Applicants are allowed to claim what they consider to be their invention.

First, present claims 1, 23, 77, 79 and 80 all recite a positive process step: "conducting a nucleic acid amplification reaction." To practice the claimed method, those of skill in the art need merely perform a nucleic acid amplification reaction (using the primer specified elsewhere in the claim). Any nucleic acid amplification reaction will do, and numerous such reactions are known. It is not seen how or why, nor has the Office Action explained how or why, those of skill in the art could misinterpret the claims. If it is a nucleic acid amplification reaction, it is covered by the claims. Applicants submit that those of skill in the art know what constitutes a nucleic acid amplification reaction. Although such reactions are broadly covered, this does not make the scope of the claims indefinite. For the same reasons, the claims are proper process claims and constitute statutory subject matter under 35 U.S.C. § 101.

The Office Action makes the error of focusing on the "use" of the template-deficient primer in the nucleic acid amplification reaction. Although such use can be, by itself, a proper method step, as discussed above, the present claims include another clear and acceptable method step. Thus, even if the recited "use" of the template-deficient primer did not constitute a proper method step, the claims would meet the requirements of 35 U.S.C. § 112, second paragraph, at least because of the method step "conducting a nucleic acid amplification reaction." For the same reasons, the claims are proper process claims and constitute statutory subject matter under 35 U.S.C. § 101.

To the extent the present rejection is based on the allegation that those of skill in the art would not know how to "use" the recited template-deficient primers in a nucleic acid amplification reaction, applicants submit that those of skill in the art are well aware of the use of primers in nucleic acid amplification reactions, both what their function is and how they are to be used. Those of skill in the art should and would use the template-deficient primers as they would any other primer in the chosen nucleic acid amplification reaction (and they would know and

understand how to do so). Because numerous nucleic acid amplification reactions (they may make use of primers in numerous different ways) are covered by the claims, it is understandable and entirely proper that specifics of the use of the recited primers are not in the claims. The law does not require that such specifics be included. Again, applicants emphasize that those of skill in the art would know what is meant and what to do. The Office Action does not establish that those of skill in the art would not know what is meant or what to do. For these additional reasons, the claims meet the requirements of 35 U.S.C. § 112, second paragraph. For the same reasons, the claims are proper process claims and constitute statutory subject matter under 35 U.S.C. § 101.

Finally, regarding the legal premise underlying the present rejection (that recitation of a "use" of something is an improper method step), applicants note that *Ex parte Porter* found the single step of "utilizing" in a claim to be definite and to be statutory subject matter. MPEP 2173.05(q). It is stated in MPEP 2173.05(q) that ". . . a claim which clearly recited the step of "utilizing" was not indefinite under 35 U.S.C. 112, second paragraph. (Claim was to "A method for unloading nonpacked, nonbridging and packed, bridging flowable particle catalyst and bead material from the opened end of a reactor tube which comprises utilizing the nozzle of claim 7.")." The preceding quote refers to claim 6 of the Porter application. *Ex parte Porter* states that "...we do not agree with the examiner that the claim is either ambiguous or non-statutory." *Ex parte Porter*, 25 U.S.P.Q.2d 1144 (1992). It is also stated "[t]he manner in which claim 6 has been drafted has been an acceptable format for years. . . Contrary to the examiner's assertion that claim 6 has no method step, the claim clearly recites the step of "utilizing." Such single – step method claims were present in *In re Kuehl* . . ." *Ex parte Porter*, 25 U.S.P.Q.2d 1144 (1992). *In re Kuehl* includes a claim stating "A hydrocarbon conversion process which comprises contacting a hydrocarbon charge under catalytic cracking conditions with the composition of claim 6." *In re Kuehl*, 475 F.2d 658, 177 U.S.P.Q. 250 (1973). Thus, it is clear that a single broad step, even a step that amounts to a "use," can be proper and statutory.

B. Rejection Under 35 U.S.C. § 102

Claims 1, 5, 8-10, 19, 22 and 77 were rejected under 35 U.S.C. § 102(a), (e) as being anticipated by Wallace (U.S. Patent No. 6,027,923) (Wallace). Applicants respectfully traverse this rejection.

Applicants first note that there appears to be some misunderstanding of what is being claimed (and of what applicants have argued). For example, focus on particular method steps of Wallace has confused a main point of distinction between the claims and Wallace.

To anticipate the claims, Wallace must disclose every element of the claimed method. The claims involve the use of a template-deficient oligonucleotide and recite specific features and properties of the oligonucleotide. Claim 1 provides "...wherein the *number and composition of template-capable nucleotides 3' of the template-deficient nucleotide* closest to the 3'end of the template-deficient oligonucleotide *is sufficient to allow the template-capable nucleotides 3' of the template-deficient nucleotide* closest to the 3' end alone *to effectively prime nucleic acid synthesis* in the nucleic acid amplification reaction" (emphasis added). A careful reading of this claim language shows that the claim identifies:

(A) a particular nucleotide in the oligonucleotide (hereinafter "nucleotide (A)", defined as "the template-deficient nucleotide closest to the 3' end of the template-deficient oligonucleotide"),

(B) a particular sub-region of the oligonucleotide (hereinafter "sub-region (B)", defined as the "nucleotides 3' of the template-deficient nucleotide closest to the 3' end of the template-deficient oligonucleotide"--that is, nucleotides 3' of nucleotide (A)), and

(C) a property of this particular sub-region (hereinafter "property (C)", wherein "the number and composition of template-capable nucleotides [in sub-region (B)] is sufficient to allow the template-capable nucleotides [in sub-region (B)] alone to effectively prime nucleic acid synthesis in the nucleic acid amplification reaction").

Note that property (C) is a property of sub-region (B) alone, not of the template-deficient oligonucleotide as a whole. This distinction is crucial. Submitted with this Response are a diagram of an example of a template-deficient oligonucleotide as claimed where nucleotide (A)

is highlighted in pink and sub-region (B) is highlighted in green (Appendix 1) and a copy of Wallace Figures 1-4 where the nucleotide analogous to nucleotide (A) is highlighted in pink and the sub-region analogous to sub-region (B) is highlighted in green (Appendix 2).

With the above in mind, applicants submit that Wallace does not disclose any oligonucleotide used in a nucleic acid amplification reaction that has a sub-region meeting the description of sub-region (B) as claimed having property (C) as claimed. In particular, the nucleotides 3' of the template-deficient nucleotide closest to the 3' end of the template-deficient oligonucleotide in the primers of Wallace (the green regions in Appendix 2) are not alone capable of effectively priming nucleic acid synthesis in the nucleic acid amplification reaction of Wallace. That is, the analogous sub-region of the primers of Wallace lacks property (C). For at least this reason, Wallace fails to anticipate the claims.

The following is a discussion of the evidence establishing that the primers of Wallace lack property (C). The fact that the 3' end regions of the Wallace primers lack property (C) is clearly established in Wallace. That is, the nucleotides 3' of the template deficient nucleotide are not sufficient to prime nucleic acid synthesis. This is established because if they were sufficient, then the primers of Wallace would produce third and higher generation primer extension (which the primer do not). See, for example, Figures 3 and 4 of Wallace showing that second generation strands (labeled 10 and 20) are not replicated because the primers cannot effectively prime replication. This is because the small portion on the second generation strands that is complementary to the primers is too short (and/or of such composition) for the primer to be able to prime replication effectively (see, for example, Wallace, col. 2, lines 49-53). This small portion corresponds to the nucleotides in the Wallace primers 3' of the template-deficient nucleotide closest to the 3' end of the Wallace primers (which makes it analogous to sub-region (B) of the claimed oligonucleotides).

Preventing these higher generation of primer extension products is a major goal of Wallace. Wallace, column 9, lines 18-25 state "[t]he use of primer that contain non-replicable and/or cleavable elements ensures that, except for primer extension products synthesized on an original template nucleic acid strand present in the starting material . . .none of the synthetic

nucleic acids produced during the process will serve as templates in subsequent rounds of primer extension." This is considered an advantage of the Wallace process as it is stated that "[s]till further advantages are presented as the products accumulate linearly and thus can be accurately quantified; the occurrence of "false positives" will be reduced in comparison with exponential processes that use newly-synthesized DNA as a template in subsequent rounds using the same primer." (Wallace, column 13, line 6-11). The above two paragraphs was a discussion of the evidence establishing that the primers of Wallace lack property (C).

For the reasons above, Wallace fails to anticipate claims 1, 5, 8-10, 19, 22 and 77.

C. Rejection Under 35 U.S.C. § 102/103

Claims 1-19, 21-23, 27, 31-45 and 77-80 were rejected under 35 U.S.C. § 102(e), or in the alternative § 103(a), as being unpatentable over Van Ness *et al.* (U.S. Patent No. 6,361,940) (Van Ness). Applicants respectfully traverse this rejection.

The rejection on page 12 states that "[w]hile agreement is reached in that Table 14 does contain some primers that do not have an abasic or modified nucleotide, Table 14, supra, clearly and explicitly teaches the incorporation of just such modified nucleotides in other primers as well as the use of said primes [sic] in amplification reactions." Applicants agree that Table 14 shows primers containing "modified nucleotides" and that some of these primers are effective at priming nucleic acid replication. However, applicants submit that none of the primers in Table 14 of Van Ness have all of the features and properties of the claimed template-deficient oligonucleotides. Table 14 of Van Ness and the surrounding text show primers that can be placed into three categories.

1. Primers that Do Not Contain Any Modified Nucleotides

H17, H14 and H11 do not contain dS (an abasic nucleotide) or any other modified nucleotide. Thus, H17, H14 and H11 do not contain a template-deficient nucleotide. These primers do not meet all of the limitations of claims 1-19, 21-23, 27, 31-45 and 77-80 of the present application.

2. Primers that Contain Abasic Nucleotides

AB1, AB2 and AB3 contain dS (an abasic nucleotide) but amplification does not occur in their presence. Thus, AB1, AB2 and AB3 have a template-deficient nucleotide but cannot effectively amplify nucleic acids in the nucleic acid amplification reaction of Van Ness (see column 4 in Table 14). More specifically, the nucleotides 3' of the template-deficient nucleotide are not sufficient to prime nucleic acid synthesis. These primers do not meet all of the limitations of claims 1-19, 21-23, 27, 31-45 and 77-80 of the present application.

3. Primers that Contain deoxyNebularine Nucleotides

DN1, DN2, DN3, DN4, DN5 and DN6 contain dN (deoxyNebularine). While dN is a "modified" nucleotide, it is not a template-deficient nucleotide. Therefore, these primers do not meet all of the limitations of claims 1-19, 21-23, 27, 31-45 and 77-80 of the present application. The ability of these primers to prime replication and amplify nucleic acids is irrelevant.

Page 11, line 20 of the present application defines template-deficient nucleotides as "...nucleotides or nucleotide analogs that (when contained in a nucleic acid molecule) cannot serve as a template for nucleic acid synthesis." Column 85, lines 39-41 of Van Ness state "[h]owever, the polymerases can read through deoxyNebularine residues present in the oligonucleotide primers." Therefore, by definition, dN is not a template-deficient nucleotide. By way of contrast, column 85, line 35 of Van Ness states "[t]hat is, when the polymerase encounters an abasic residue, chain extension is terminated." Chain extension is not terminated with dN. dN is a base analog (see col. 21, lines 23-27) , which is defined in Van Ness with the following: "a 'base analog' or 'base analog residue' in an oligonucleotide refers to a molecular fragment that includes a ribofuranose sugar and is substituted at the beta anomeric position with a group similar to that of at least one of the A,C,G,T or U bases, so that a polymerase will read through the base analog..."(Van Ness, column 21, lines 15-21). Thus, base analogs of Van Ness cannot be template-deficient nucleotides.

As Van Ness does not meet the limitation of the present claims that the primers contain a template-deficient nucleotide, the position of the modified nucleotide (i.e. non-template-deficient nucleotide) in a primer in Van Ness does not matter; nor does the fact that these primers result in

amplification. Therefore, Van Ness does not disclose primers that meet the limitations of the claims of the present application.

Summarizing, the H17, H14 and H11 primers do not contain a template-deficient nucleotide, the AB1, AB2 and AB3 primers do not have the required "effectively prime" property (property (C) discussed above), and the DN1, DN2, DN3, DN4, DN5 and DN6 primers do not contain a template-deficient nucleotide. Thus, none of the primers in Table 14 of Van Ness have all of the features and properties required by the present claims.

Van Ness provides no motivation to use template-deficient nucleotides in a primer where nucleotides 3' of the template-deficient nucleotide are sufficient to prime nucleic acid synthesis. The use of abasic and modified nucleotides in Van Ness is for the purpose of creating a mismatch between the primer and the template that will improve the specificity and accuracy of PCR priming. Van Ness does not teach the placement of the template-deficient nucleotide and the template-capable nucleotides 3' to the template-deficient nucleotide, along with their number and composition, with the purpose of the 3' template-capable nucleotides being capable of priming nucleic acid amplification on their own. Thus, those of ordinary skill in the art reading Van Ness would not be directed or guided to make the particular oligonucleotides used in the claimed method. Even if priming is improved in Van Ness, it is not taught that the nucleotides 3' to the template-deficient nucleotides are sufficient to do so based upon the number and composition of those nucleotides. More specifically, the improved priming effect sought by Van Ness would not lead those of skill in the art to place template-deficient oligonucleotides where the present claims require them. Therefore, the present application is patentable over Van Ness.

Conclusion

Pursuant to the above amendments and remarks, reconsideration and allowance of the pending application is believed to be warranted. The Examiner is invited and encouraged to directly contact the undersigned if such contact may enhance the efficient prosecution of this application to issue.

No fees are believed due. However, the Commissioner is hereby authorized to charge any fees which may be required, or credit any overpayment to Deposit Account No. 14-0629.

Respectfully submitted,

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I hereby certify that this correspondence, including any items indicated as attached or included, is being deposited with the United States Postal Service as first class mail in an envelope addressed to: MAIL STOP AF, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on the date indicated below.

Robert A. Hodges — Date 10/16/2003

Appendix 1